

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 028622-0108

In re patent application of
Jungblut *et al.*

Group Art Unit: 1645

Serial No. 09/890,339

Examiner: R. Swartz

Filed: 03/12/2002

For: Identification of Specific Differentially Expressed Mycobacterial Antigens

DECLARATION UNDER 37 CFR § 1.132

Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

I, Stefan H.E. Kaufmann, hereby declare:

1. I am an inventor of the captioned '339 application. I have worked in the field of immunology for over 25 years. I have over 500 publications with a huge number of these papers in the field of immunology. I received a Ph.D. in 1977 from the University of Mainz. In 1993, I became the Founding Director of the Max Planck Institute for Infection Biology and I am presently the Director of the Department of Immunology at the Max Planck Institute. Attached is my CV to further explain my experience and background.
2. I have read and understood the Office Action dated July 19, 2004, and particularly the Examiner's comments regarding the lack of enablement in the specification for the identification and isolation of the claimed vaccines.
3. In response to the Examiner's comments on page 5 of the Office Action that the specification does not reasonably provide enablement for vaccines, I provide the following information to show that the claimed vaccine inventions are enabled by the specification of the '339 application. My research group has conducted additional studies using proteins Rv0068 and Rv3407, and methods described in the '339 application to show that the vaccine claims enumerated in the application were enabled as of the filing date of the application.

4. BALB/c mice were bred by my laboratory. Animals were kept under specific pathogen-free (SPF) conditions and fed autoclaved food and water *ad libitum*. In these experiments, female mice were used at 8 weeks of age. Groups of at least 5 mice were used in all experiments.

Bacterial strains were grown according to the protocol of Example 1, page 29 of the specification. In short, *M. bovis* BCG strain Danish 1331 (Statens Serum Institute, Copenhagen, Danmark) was cultured in Dubos broth base (Difco, Detroit, MI, U.S.A.) supplemented with Dubos medium albumin (Difco) at 37°C with shaking until bacterial growth reached an optical density (OD₆₀₀) of approximately 0.7 (equivalent to a cell density of approximately 10⁸ cells per ml). *M. tuberculosis* H37Rv was grown at 37°C on Middlebrook 7H9 agar (Difco) supplemented with oleic acid, albumin, dextrose and catalase (OADC) enrichment 1339 (Difco) after passage through mice, and subsequently in Middlebrook 7H9 liquid medium containing ADC enrichment (Difco) under shaking until bacterial growth reached an OD₆₀₀ of approximately 0.7. Mycobacteria were harvested by centrifugation, washed with PBS without Ca²⁺, and maintained in 10% glycerol at -70°C until use. Cellular proteins were prepared from whole cell lysates. The sonicate was stored at -70°C. P815 mastocytoma cells were obtained from the American Type Culture Collection (ATCC, Manassas, VA, USA) and cultured in RPMI 1640 (Life Technologies, Karlsruhe, Germany) supplemented with 10% FCS, penicillin (100 U/ml), streptomycin (100 U/ml), and 2-mercaptoethanol (RP10).

Preparation of vectors for vaccination was performed according to methods described in the '339 application. Protocols for the production of recombinant proteins are provided in the specification on pages 10-11 and 13-15. In short, the *M. tuberculosis* genes Rv3407 and Rv0068 were cloned into the DNA vaccine vector pCMVtPA (Chiron-Behring, Emeryville, USA). This vaccine vector encodes DNA vaccine antigens as tPA leader peptide fusion proteins under the control of the CMV promoter. The DNA vaccine antigens were amplified by PCR reaction using *M. tuberculosis* H37Rv chromosomal DNA as template with gene specific oligonucleotide primers containing additional cloning sites at their 5' ends. PCR amplification was carried out in an Eppendorf Mastercycler (Eppendorf, Hamburg, Germany) for 30 cycles using the following conditions: 94°C for 1 min, 56°C for 45 s, and 72°C for 1 min. The amplification products were purified by agarose gel electrophoresis and sub-cloned into the *Sma*I restriction site of the cloning vector pUC18. The resulting plasmids carrying the subcloned PCR products were identified by restriction endonuclease digestion and the inserted sequences were confirmed by

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DNA sequencing. The verified sequences were cleaved from the pUC18 backbone by restriction endonuclease digestion specific for the incorporated 5' sites of the PCR products and subsequently ligated to the DNA vaccine vector pCMVtPA resulting in the conclusive DNA vaccine constructs. The inserted sequences were verified by DNA sequencing. For DNA vaccination experiments, the DNA vaccines encoding *M. tuberculosis* unique antigens were purified with the EndoFree Plasmid Purification kit (Qiagen, Hilden, Germany).

Vaccination was accomplished through procedures described on pages 19-22 of the '339 application. In this case, BALB/c mice were immunized 3 times intramuscularly (i.m.) with 100 μ g DNA per mouse (50 μ g per quadricep) at 21 d intervals. DNA vaccines encoding for *M. tuberculosis* unique antigens were tested. As a control, mice were vaccinated with 10⁶ *M. bovis* BCG by intravenous (i.v.) injection into the tail vain. As known in the art and detailed in the application as filed, *M. bovis* BCG is a avirulent strain of *M. bovis* and commonly used as a tuberculosis vaccine. Naïve mice were used as negative control. At 120 d post BCG vaccination and 21 d after the last booster immunization with DNA vaccine candidates Rv3407 and Rv0068, mice were challenge-infected with *M. tuberculosis* H37Rv by an aerosol exposure system (Glas-Col, Terre Haute, U.S.A.) with an infection dose of 200 bacilli per lung. Protection was monitored on d 14, d 30, and d 60 post infection (pi) by enumeration of bacterial colony forming units (CFU) in lungs by plating serially diluted organ homogenates on Middlebrook 7H9 agar.

Methods of using computer predictions for antigenicity may be found on page 10 in the specification. In this case, possible MHC I immunogenic peptide epitopes for the antigen Rv3407 were computed by the program 'MHC-I Antigenic Peptide Processing Prediction' (MAPPP).

A combination of the proteasomal processing software FRAGPREDICT and PAProC with the MHC binding ligand predictions SYFPEITHI and BIMAS in the expert mode of MAPPP were used. Parameters for FRAGPREDICT were set at 0.5 (minimal residue cleavage probability and minimal fragment cleavage probability) and at 0.15 in PAProC. The inventors used the murine haplotypes H2Kd, H2Dd and H2Ld and a fragment length of 8 to 10 amino acids. The threshold was set at an over-all-score of 0.84 for the gene product Rv3407. All peptides predicted were either 9 or 10mers. Purified peptides (Jerini, Berlin, Germany) were used in ELISpot assay with splenocytes of vaccinated and control animals.

Methods of detection by assays, including immunoassays are described in the specification on pages 22-24. Here, frequencies of IFN- γ -secreting T lymphocytes with specificity for Rv3407 MHC I epitopes were determined by a modified enzyme-linked immunospots (ELISpot) technique. Briefly, 96-well Millititer HA nitrocellulose plates (Millipore, Bedford, U.S.A.) were coated with 5 mg/ml of the anti-mouse IFN- γ mAb R4 (B&D, Heidelberg, Germany) in 100 μ l of carbonate buffer, pH 9.6. After overnight incubation at 4°C, plates were washed twice with PBS and blocked at 37°C for 2 h with 100 μ l 1% BSA in PBS. Splenocytes (10^5) from vaccinated mice were pulsed with 10 μ g/ml specific peptides and then cultured in 100 μ l RP10 medium per well. The P815 cells were coated with 10 μ g/ml peptides in PBS at 37°C for 1 h and then washed twice with RP10. Concanavalin A (ConA) stimulated splenocytes served as positive control. Coated or uncoated P815 cells (10^5) were added to splenocytes in 100 μ l of RP10, and after 20 h incubation at 37°C, 5% CO₂ in the presence of 30 U/ml IL-2, the plates were washed 10 times with 0.05% Tween 20 in PBS (washing buffer). To detect IFN- γ positive spots, 0.25 μ g/ml biotinylated anti-mouse IFN- γ mAb XMG1.2 (B&D) in 100 μ l washing buffer was added and incubated at 37°C for 2 h. Plates were washed 10 times and incubated for 1 h at 37°C in 100 μ l of a 1/20,000 dilution of alkaline phosphatase-coupled streptavidin (B&D). After 5 washes, spots of IFN- γ secreting cells were visualized by adding 50 μ l of the ready-to-use substrate 5-Bromo-4-Chloro-3-Indolyl Phosphate/NitroBlue Tetrazolium (BCIP/NBT, Sigma, St. Louis, U.S.A.) dissolved in water. The reaction was stopped after 15 min at 37°C by several washes with distilled water. After drying, spots were counted under a dissecting microscope at 3-fold magnification or they were counted automatically with a Bioreader 2000 (Biosys, Karpen, Germany). Frequencies of peptide-specific T cells are expressed as spot forming units (SFU) of IFN- γ secreting cells per 10^5 splenocytes.

The detection of Rv3407-specific MHC class II-restricted T cells is provided below. To induce specific cytokine secretion by antigen-specific CD4 T cells, 10^5 splenocytes per well were stimulated with 10 μ g/ml heat-denatured protein lysate of H37Rv in 100 μ l RP10 for 3 d. The J774A.1 macrophage-like cells were pulsed with 10 μ g/ml heat-denatured protein lysate of H37Rv in RP10 at 37°C for 1 h and subsequently washed twice with RP10. Coated or uncoated J774A.1 cells (10^5) were added to splenocytes in 100 μ l RP10 and after 20 h incubation at 37°C, 5% CO₂ in the presence of 30 U/ml IL-2, plates were washed 10 times with washing buffer.

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Plates for IFN- γ -detection were prepared as described above. Incubation times and detection followed the ELISpot protocol for MHC class I- restricted T cells.

Significance of differences was calculated according to the Student's *t* test and the nonparametric two-tailed Mann Whitney test with a confidence interval at 95% and a *P value* < 0.05 considered significant. The individual groups in each experiments contained either 5 to 6 mice for the initial screening procedure or at least 7 and, occasionally, 10 mice per time point for verification. Mean values of in vitro studies are based on 3 replicates.

5. The vaccine candidate Rv0068 induced protection particularly at day 60 post challenge (see appended Fig.1). The corresponding protection was documented by the decline of the "bacterial colony forming unity" (CFU).

The vaccine candidate Rv3407 induced protection at all determined time points, with high significance at day 14 as well as at day 30 post aerosol challenge (Fig. 2). Verification of the experiments revealed that Rv3407 showed appreciable levels of protection comparable to a control Ag85 (Rv3804) at day 30 and day 60 post challenge (Fig. 3). It is of note that Ag85 is one of the most efficacious DNA vaccine candidates currently known. In the experiment shown in Fig. 3, BCG vaccination, which was used as positive control, provided protection of 0.8 log at both time points whereas the empty vector control resulted in no protection. The Rv3407 encoding DNA vaccine induced comparable protection (0.7 log) at day 30 post-challenge, and then slightly decreased to 0.5 log by day 60. Accordingly, Rv3407 shows protection which is at least comparable to one of the most efficacious candidates (Ag85) known in the art.

In a further set of experiments, antigen-specific IFN- γ secretion by spleen cells from vaccinated and control mice was analyzed by ELISpot assay (Fig. 4). CD4 T cell responses were stimulated by soluble protein lysate of *M. tuberculosis*; CD8 T cell responses were induced by peptides representing predicted dominant MHC I epitopes. The prediction was done by MAPPP, which combines existing prediction tools for proteasomal processing and MHC I anchoring. This combination enhances the accuracy and the significance of the prediction. IFN- γ responses were measured 28 and 35 d after the second booster vaccination.

At day 28 post vaccination, the vaccine candidate Rv3407 induced IFN- γ production in both CD4 and CD8 T cells. Rv3407 induced specific IFN- γ responses with both, peptide and lysate, although at this time point, only 1 of the 2 predicted peptides induced IFN- γ secretion

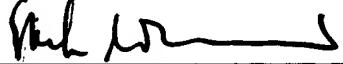
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after restimulation. Consistent protection induced by Rv3407 correlated well with the capacity to induce IFN- γ responses at early as well as late time points. Accordingly, Rv3407 also provides for immunological responses on the protein and peptide level.

Consistent with the robust protection induced by Rv3407, profound IFN- γ production and low antibody responses were observed. It is generally accepted that both CD4 and CD8 T lymphocytes are required for protective immunity against tuberculosis. In accordance with the profound protection induced by Rv3407, IFN- γ was produced by CD4 and CD8 T cells.

Accordingly, not only protection experiments but also vaccination analysis documents that antigen Rv3407 is able to induce significant protection.

6. I hereby declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

By: 
Prof. Stefan H.E. Kaufmann

Date: 13 November 2004

Prof. Stefan H. E. Kaufmann
- Director -
Max-Planck-Institute for Infection Biology



CURRICULUM VITAE

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Personal Data

Born, June 8, 1948, Ludwigshafen, Germany
German citizen
Married, two children

Academic Education

- Habilitation in Microbiology and Immunology, Free University, Berlin, 1981
Title: "Characterization of T lymphocytes involved in immunity to facultative intracellular bacteria using serologically selected and cloned T-cell populations"
- Dr. rer. nat. (Ph.D.), Johannes Gutenberg University, Mainz, 1977
Title: "Alternative pathways in corticosteroid biosynthesis" (with distinction, summa cum laude)
- Diploma in Biology, Johannes Gutenberg University, Mainz, 1973

Positions

- Founding Director and Member at the Max-Planck-Institute for Infection Biology, Berlin, 1993 to present
- Member of the Max-Planck-Society, 1993 to present
- Acting Director of the Max-Planck-Institute for Infection Biology, Berlin, September 2001 to September 2003
- Honorary professor at the Universitätsklinikum Benjamin Franklin, Medical Faculty of the Free University, 2003 to present
- Professor (apl.) at the Charité, Medical Faculty of the Humboldt University Berlin, March 1998 to present
- Caretaker Director of the Department of Immunology, University of Ulm, May 1998-May 1999
- Full Professor and Chair, Department of Immunology, University of Ulm, August 1991-April 1998

- Professor for Medical Microbiology and Immunology, Department of Medical Microbiology and Immunology, University of Ulm, 1987-1991
- Staff Scientist, Max-Planck-Institute for Immunobiology, Freiburg, 1982-1987
- Docent, Institute for Medical Microbiology, Free University, Berlin, 1981-1987
- University Assistant (C1), Institute for Medical Microbiology, Free University, Berlin, 1982
- Assistant Professor, Institute for Medical Microbiology, Free University, Berlin, 1978-1981
- Scientific Assistant, Institute for Medical Microbiology, Ruhr University, Bochum, 1976-1978

Extramural financial support

- WHO-IMMTUB, 1983-1990
- WHO-IMMLEP, 1987-1993
- EC-India Science and Technology Cooperation Program, 1989-1992
- German Leprosy Relief Association, 1987-1992
- German Research Society (SFB 322 "Lympho-Hemopoiesis" Project B7), 1986-1997
- Landesschwerpunkt, 1989-1994
- German Research Society (SFB 322 "Lympho-Hemopoiesis", Project B10), 1992-1997
- Graduiertenkolleg "Biomolecular Medicine", 1992-1998
- German Research Society (DFG Ka 573/3-1/2), 1993-1998
- BMBF Joint Project "Mycobacterial Infections", 1994-2001
- German Leprosy Relief Association, 1996-1999
- WHO-GPV, VRD, 1999-2002
- Industry cooperation (Chiron Behring Emeryville, U.S.A.) "Development of a vaccine against tuberculosis", 1999-2001
- German Research Society (SFB 421) "Protektive und Pathologische Folgen der Antigenverarbeitung" (Project A4), 1999 to present
- EC Thematic Network "European Bacterial Proteomics" (QLRT-1999-31536) (together with Dr. P. Jungblut), 2000-2003
- EC Cluster "TB Vaccine" (QLRT-PL1999-01093), 2000-2004
- Project KA 573/4-1 in the DFG Priority Program "Novel Vaccination Strategies", 2000 to present
- EC Project "X-TB" (QLRT-2000-02018) (together with Dr. P. Jungblut), 2001 to present
- BMBF Joint Project "Genomics of Bacterial Pathogens", 2001 to present
- BMBF Joint Project "New Methods for the Generation of Complete Bacterial Proteomes" (together with Dr. P. Jungblut), 2001 to present
- Industry cooperation (Chiron Behring Marburg, Germany) Phase I Vaccine Trial against Helicobacter pylori, 2001-2003
- DFG Clinical research unit "Immunpathogenese und Interventionsstrategien bei mukosalen Infektionen" (project MI 476/2-1, together with Dr. H.W. Mitterücker) 2002 to present
- BMBF Competence Network "Strukturgenomik von biologischen Makromolekülen aus dem *M. tuberculosis* Genom" (together with Dr. J. Mattow), 2002 to present
- BMBF Competence Network "Proteomweite Analyse membrangebundener Proteine" (together with Dr. A. Kahnert), 2003 to present
- BMBF Competence Network CAPNETZ "Community acquired pneumonia" (together with Dr. J. Zerrahn), 2001 to present
- German Research Society (SFB 633) "Induktion und Modulation T-zellvermittelter Immunreaktionen im Gastrointestinaltrakt", Project B5, 2003 to present.
- EFRE/IBB Innovation support program of Berlin Senate "Molekulardiagnostische Microarrays" (together with Dr. H.-J. Mollenkopf), 2003 to present
- EU Integrated Project TB VAC (LSHP-CT-2003-503367), 2004 to present
- EU Integrated Project MUVAPE (LSHP-CT-2003-503240), 2004 to present

- EU Integrated Coordination Action "ANTHRAX EURONET" (SSPE-CT-2003-503616), mit Dr. A. Ozin), 2004 to present
- EU Project Marie Curie RTN "MICROBAN" (MRTN-CT-2003-504227), 2004 to present

Other Experiences

- Biohazard safety committee, University of Ulm, 1992-1996
- Radioactivity safety committee, University of Ulm, 1987-1998
- Radioactivity safety committee, Max-Planck-Institute for Immunobiology, Freiburg, 1982-1987
- Biohazard safety committee, Max-Planck-Institute for Immunobiology, Freiburg, 1985-1987
- Bacteriological diagnostics, Free University, Berlin, 1978-1982
- Radioactivity safety committee, Free University, Berlin, 1979-1982

Recognition and Awards

- Honorary Member of the World Innovation Foundation, July 2004
- Eijkman Medal and Lecture, Utrecht, April 2004
- Dr. Friedrich Sasse Price 1999/2000/2001, September 24, 2003, received as President of the German Society for Immunology
- Highly Cited Researcher 1981-1999 (category Immunology), Institute for Scientific Information, 2001
- 1996 Erwin Neter Memorial Lecture of the American Society for Microbiology
- Hauptpreis der Deutschen Gesellschaft für Hygiene und Mikrobiologie, September 27th, 1993
- Pettenkofer-Preis, December 2nd, 1992
- Dr. Robert Pfleger-Preis, July 10th, 1992
- Merckle Forschungspreis, November 4th, 1991
- Smith Kline Beecham Wissenschaftspreis, July 7th, 1991
- Aronson Preis des Landes Berlin, March 8th, 1988
- A.Krupp Förderpreis für junge Hochschullehrer, June 24th, 1987
- Förderpreis der Deutschen Gesellschaft für Hygiene und Mikrobiologie, October 10th, 1983
- Dr. Friedrich Sasse Price, March 27th, 1981

Editorial Boards

- "Immunobiology" (Editorial Board), 1984 to present
- "Microbial Pathogenesis" (Editorial Board), 1985 to present
- "Infection and Immunity" (Editorial Board), 1987-1994
- "European Journal of Immunology" (Editorial Board), 1988 to present
- "International Immunology" (Transmitting Editor), 1989 to present
- "Tropical Medicine and Parasitology" Editorial Board), 1989
- "Journal of Infectious Diseases" (Editorial Advisory Board), 1989-1998
- "Zentralblatt fuer Bakteriologie, Mikrobiologie und Hygiene" Abt. A (Advisory Board), 1990-1992
- "Medical Microbiology and Immunology" (Editorial Board), 1991-2001
- "Journal of Immunology" (Associate Editor), 1991-1995
- "International Archives of Allergy and Immunology" (Associate Editor), 1991-1994
- "Immunology Letters" (Editorial Board), 1992-1999

- "Trends in Microbiology" (Editorial Board), 1992 to present
- "Zentralblatt fuer Bakteriologie" (Editor), 1993-1999
- "European Research and Development Database" (Editorial Board), 1993
- "Journal of Molecular Medicine (JMM)" (Editorial Board), 1995 to present
- "Infection and Immunity" (Editor), 1995-2004
- "Journal of the International Union against Tuberculosis and Lung Disease" (Editorial Board), 1995 to present
- "Cell Stress & Chaperones" (Editorial Board), 1995-2000
- "Immunity" (Editorial Board), 1996-1998
- "Bulletin de l'Institut Pasteur: Research in Infectious Diseases" (Deputy Editor), 1996-1998
- "Cellular Immunology" (Editorial Board), 1996 to present
- "Encyclopedia of Life Sciences" (Editorial Advisory Board), 1997
- "Microbes and Infection" (formerly "Bulletin de l'Institut Pasteur", "Research in Virology" and "Research in Immunology") (Editor in Chief), 1998 to present
- "FEMS Immunology and Medical Microbiology" (Receiving Editor) 1999
- Charter member "inSight Editorial Board", 1999 to present
- "International Journal of Medical Microbiology" (International Advisory Board), 2000 to present
- Corresponding member of the Editorial Committee "Annual Review of Immunology", 2000-2002
- Faculty member "Faculty of 1000", 2001 to present
- Forum Editor "Microbes and Infection", 2002 to present
- Member Editorial Academy "International Journal of Oncology", 2002
- Section Editor "Tuberculosis", 2003 to present
- "Immunology Letters" (Editorial Board), 2003 to present
- Birkhäuser Book Series on "Advances in Infectious Diseases" (Editorial Board), 2003 to present
- "Current Immunology Reviews" (Editorial Board Member), 2004 to present
- Corresponding Editor "Annual Review of Immunology", 2004 –
- "BMC Immunology" (Editorial Board Member), 2004-

Committee Assignments

National:

- Scientific advisor of the German Research Society (DFG) "Chronic Inflammation" (SFB), 1985
- Scientific advisor of the German Ministry for Science and Technology, "Diagnostic Methods in Microbiology", 1986
- Scientific advisor of the German Research Society (DFG) "Molecular and Immunologic Mechanisms of Host-Parasite-Interactions", 1987-1994
- Scientific advisor of the German Ministry for Science and Technology, "AIDS", 1987-1994
- Member of the Vaccine-Commission at the German National Institute of Health, 1989-1994
- Member of the scientific board of the Sonderforschungsbereich 322 "Lympho-Hemopoiesis", 1989-1997
- Scientific advisor of the German Research Society (DFG) "Gastrointestinal barriers" (SFB), 1989
- Chairman of the Landesschwerpunkt "Chronische Infektionskrankheiten", 1990-1994
- Scientific advisor of the German Research Society (DFG) "Immune Mechanisms in Infection, Inflammation and Autoimmunity" (SFB), 1990
- Scientific board "Bernhard Nocht Institute for Tropical Medicine", Hamburg, 1991-1995
- Scientific board "Max-Planck-Institute for Biology", Tübingen, 1991

- Member of the Evaluation Board "Graduierten-Kolleg" of the German Research Society (DFG), 1991
- Chairman of the Sonderforschungsbereich 322 "Lympho-Hemopoiesis", 1992-1997
- Scientific advisor of the German Research Society (DFG) "Molecular cell biology of the heat shock response", 1992
- Scientific expert for "Medical Microbiology, Virology, Immunology, Hygiene", German Research Society (DFG) 1992-2000
- Member of the scientific board of the Graduiertenkolleg "Biomolecular Medicine", 1992-1997
- Member of the Commission "Infektionsepidemiologie" of the Ministry of Health and the German Ministry for Culture, Science, Research and Technology, 1995
- Member of the Commission of the Joint Project "Infectious Diseases Today - Prevention, Diagnostic and Therapy" of the Senate for Health, Berlin, 1995
- Member of the Scientific Board of the Interdisciplinary Center for Clinical Research, Cologne, 1995 to present
- Member of the Scientific Advisory Board of the Robert Koch-Institute, Berlin, 1998 to present
- Member of the Scientific Board of the Sonderforschungsbereich 421 "Protektive und pathologische Folgen der Antigenverarbeitung", 1998 to present
- Member of the Board of the German Society for Immunology, 1999 to present
- Coordinator of the German Research Society (DFG) program "Neue Vakzinierungsstrategien", 1999 to present
- Scientific Advisor of the BMBF initiative "Einrichtung eines Managementsystems für die Entwicklung von Impfstoffen", 1999-2002
- Vice president of the German Society for Immunology (DGfI), 2000-2002
- President of the German Society for Immunology (DGfI), 2003-2004
- Member of the Scientific Board of the Robert-Koch Foundation, 2001 to present
- Member of the Board of the Berlin Medical Society, 2001 to present
- Member of the Board of the Berlin Brandenburgischen Akademie der Wissenschaften, 2001 to present
- Member of the Scientific Board of the Gesellschaft für Strahlenforschung Munich, 2002 to present
- Member of the Scientific Board of the Hans-Knöll-Institut für Naturstoff-Forschung Jena, 2003 to present
- Chair of the Advisory Board of the Vaccine Project Management GmbH, 2003 to present
- Board member of the initiative of extra-university scientific institutions of Berlin "WissenSchaftZukunft", 2003 to present
- Member of the Executive Committee MTB Structural Proteomics, 2003 to present
- Member of the Scientific Board of the Sonderforschungsbereich 633 "Induktion und Modulation T-zellvermittelter Immunreaktionen im Gastrointestinaltrakt", 2003 to present
- Member of the Executive Committee of the Robert Koch Foundation, 2003 to present
- Mentor of the Mentoring Programm for Scientific Journalism for Young Scientists of the Bertelsmann Stiftung, BASF Aktiengesellschaft und Volkswagenstiftung, 2003 to present
- Interim Chair of the Scientific Board of the Gesellschaft für Strahlenforschung, Munich, 2004
- Chair of the Scientific Board of the Gesellschaft für Strahlenforschung, Munich, 2004 to present

International:

- Scientific advisor of the World Health Organization "Immunology of Tuberculosis Program", 1983-1991
- Scientific advisor of the EU research programme "Science and Technology for Development", 1988-1992
- Scientific advisor of the EU research programme "International Scientific Cooperation, Health Sciences", 1989-1991

- Chairman, Scientific Advisory Board of the EU research programme "International Cooperation, Health Sciences", 1991-1992
- Research Expert Discipline Core Group, ILEP (International Organization of Leprosy Relief Associations) 1991
- Scientific expert of the SAGE-Group, World Health Organization (WHO), 1992-1994
- Secretary-General of the European Federation of Immunological Societies, 1992-1995
- Member of the IMMYC Sub-Committee of WHO on "Mycobacterial Antigen Production and Data Base", 1992
- Scientific advisor of the German-Israeli Foundation for Scientific Research & Development, 1994-2002
- International scientific advisor of the Belgian Center for Inter-university Vaccine Research, 1995 to 2000
- Member of the Scientific Advisory Board "Robert Koch - Minerva Center for Research in Autoimmune Diseases", 1996
- Scientific advisor of the Scuola Superiore d'Immunologia Ruggero Cappellini, 1997 to present
- Scientific advisor of the NIH Programme "Challenge Grants: Joint Ventures in Biomedicine and Biotechnology" 1999
- Member of the Scientific Advisory Group of the International Vaccine Institute, Seoul, Korea, 2000 to present
- Member of the Scientific Advisory Board of Innate Pharma SA, Marseille, 2000 to present
- Member of the Human Frontier Science Program Fellowship Review Committee, 2001
- Member of the R & D Expert Group on Countering the Effects of Biological and Chemical Terrorism (DG RTD – Research Directorate General) 2001 to present
- Vice president (President Elect) of the European Federation of Immunological Societies (EFIS), 2003 to present
- Member of the Scientific Advisory Board of the Novartis Institute for Tropical Diseases, Singapore, 2003 to present
- Member of the Governing Council of the International Union of Immunological Societies, 2004 to present
- 15th European Congress of Immunology and First Joint Meeting of European National Societies of Immunology, September 6-9, 2006, Paris (Member of the Scientific Program Committee and of the Promotion Committee)

Professional Societies

- German Society for Immunology
- German Society for Hygiene and Microbiology
- American Society for Microbiology
- European Network of Immunology Institutes
- Microbiology Society of Berlin
- Society for Mucosal Immunology
- Berlin-Brandenburgische Akademie der Wissenschaften
- American Academy of Microbiology
- Deutsche Akademie der Naturforscher Leopoldina
- International Academy of Sciences of Nature and Society
- Medical Society of Berlin
- European Academy of Sciences

Publication record Stefan H.E. Kaufmann (recent publications only, starting 2000)

Originals

- Mittrücker H W, Raupach B, Köhler A, **Kaufmann S H E**. Role of B lymphocytes in protective immunity against *Salmonella typhimurium* infection. *J. Immunol.* 2000; 164:1648-1652.
- Mittrücker H W, Köhler A, **Kaufmann S H E**. Substantial in vivo proliferation of CD4⁺ and CD8⁺ T lymphocytes during secondary *Listeria monocytogenes* infection. *Eur. J. Immunol.* 2000; 30:1053-1059.
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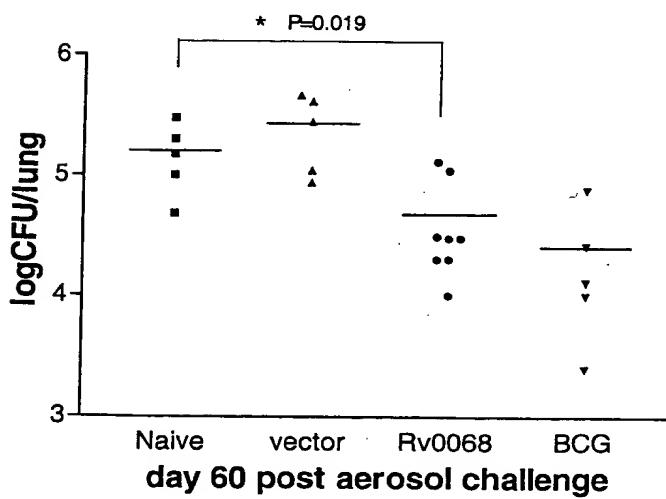
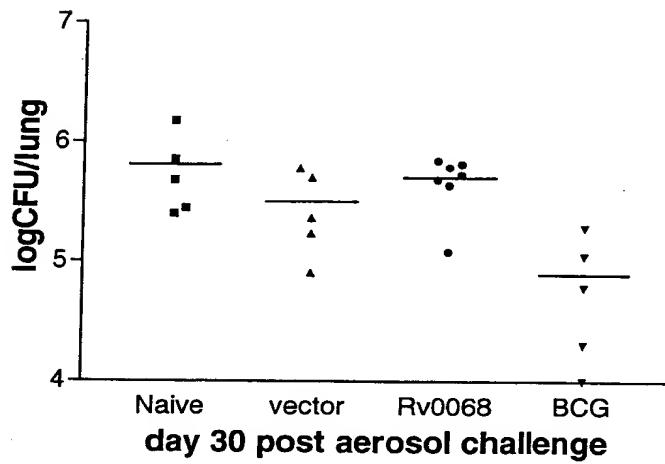
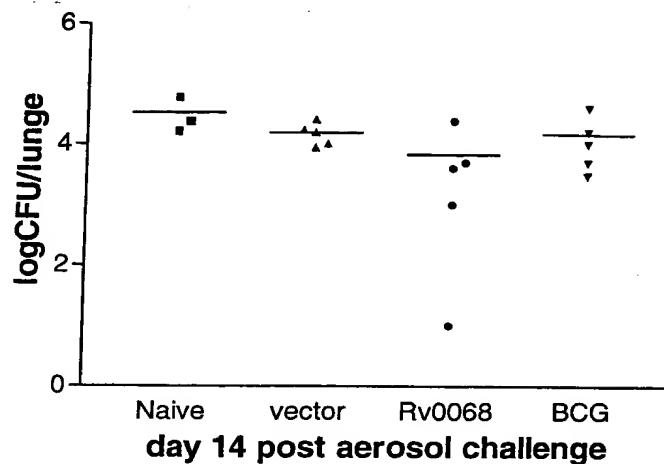


Fig. 1

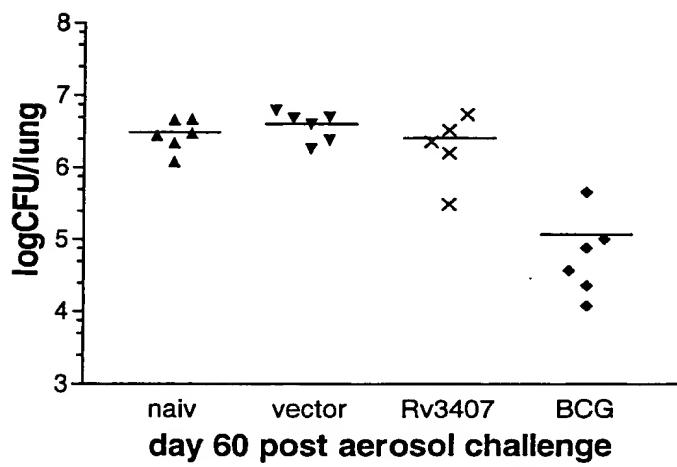
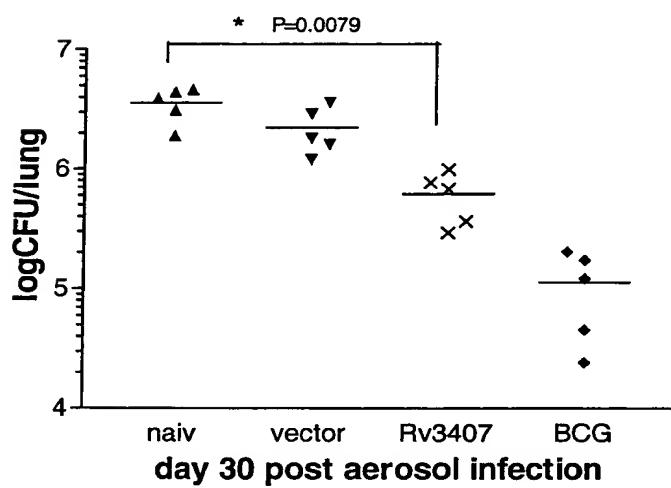
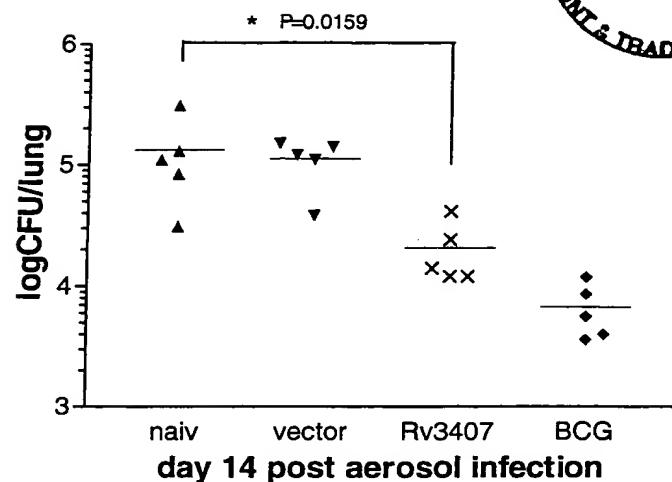
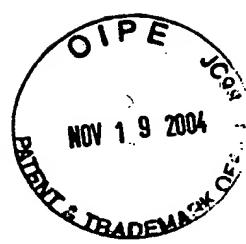


Fig. 2

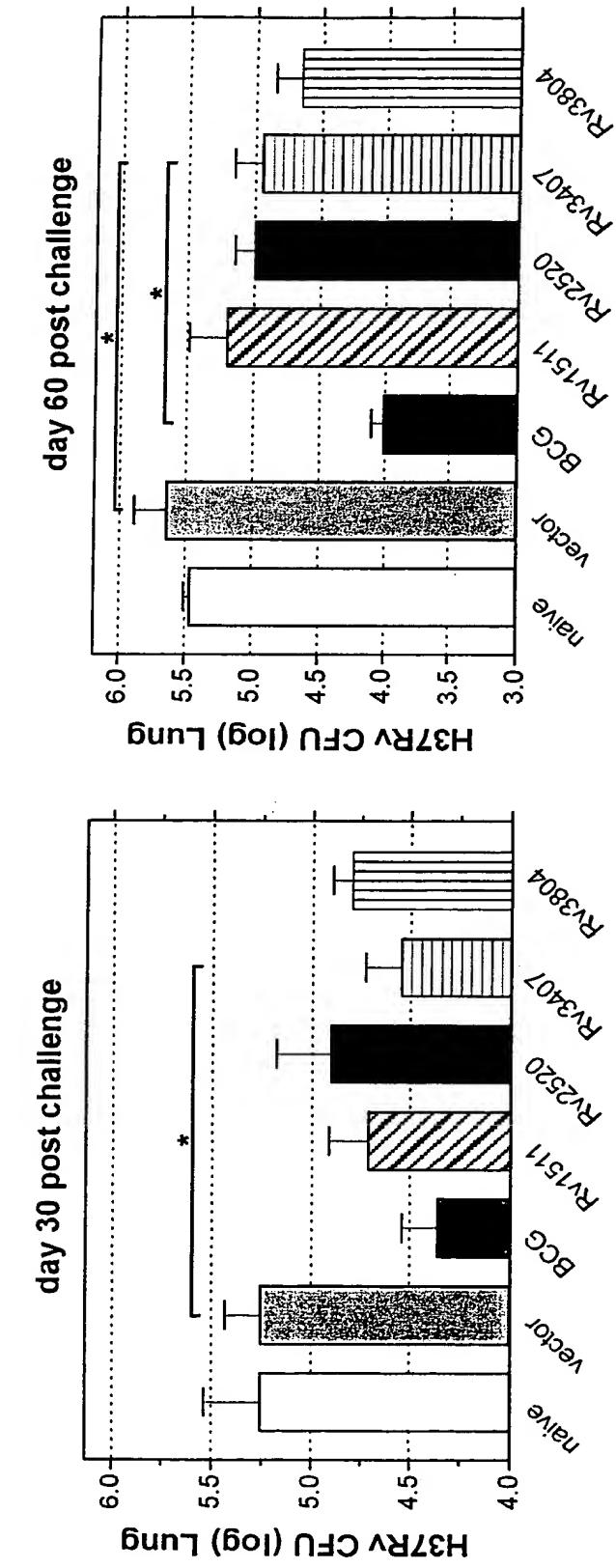
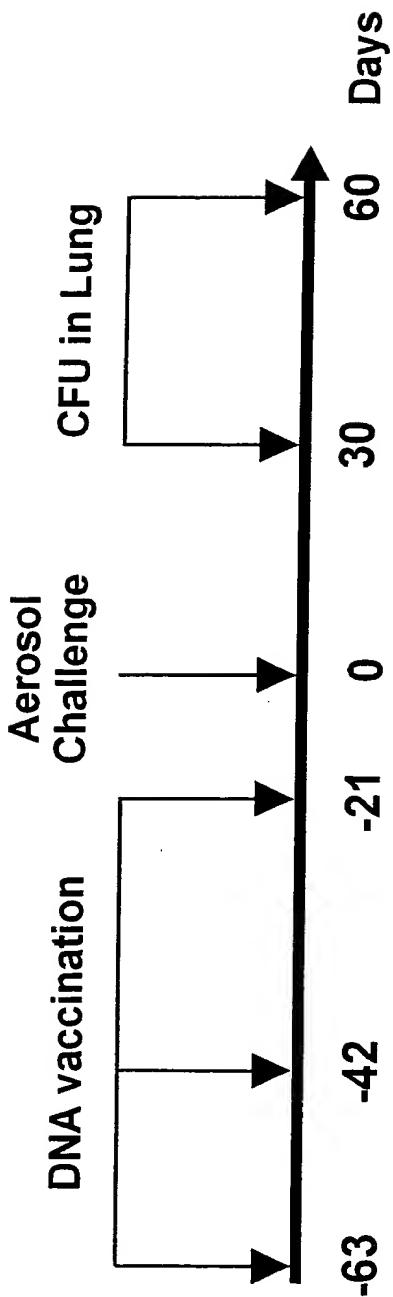
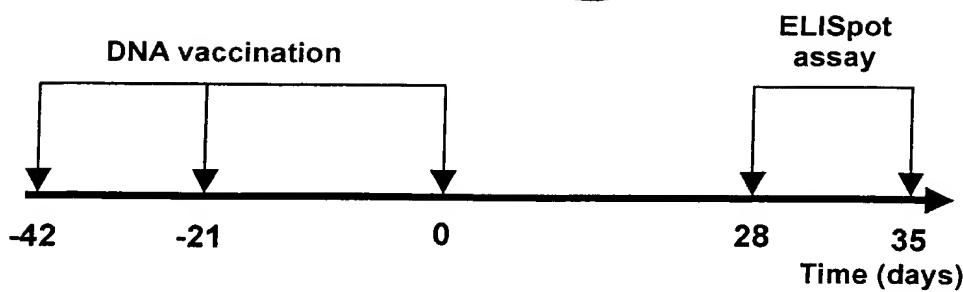
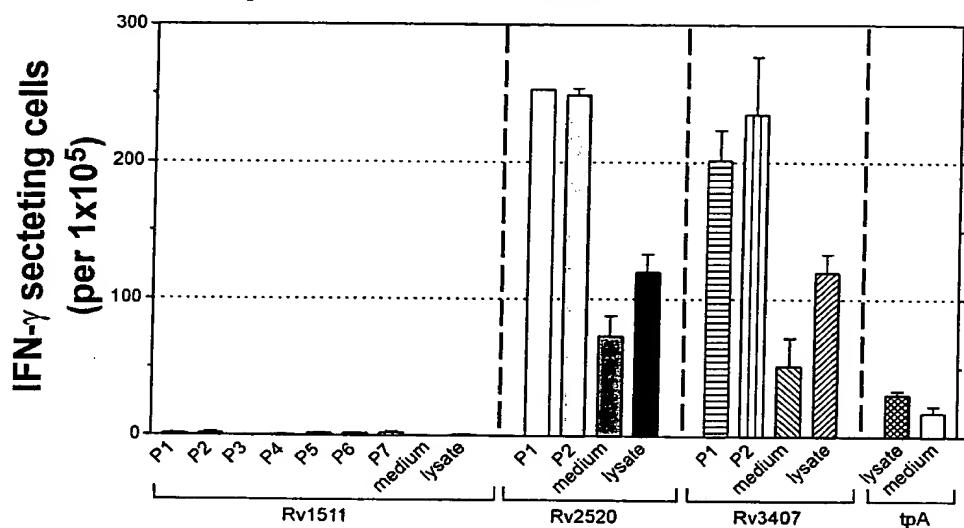


Fig. 3

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d 28 post DNA vaccination



d 35 post DNA vaccination

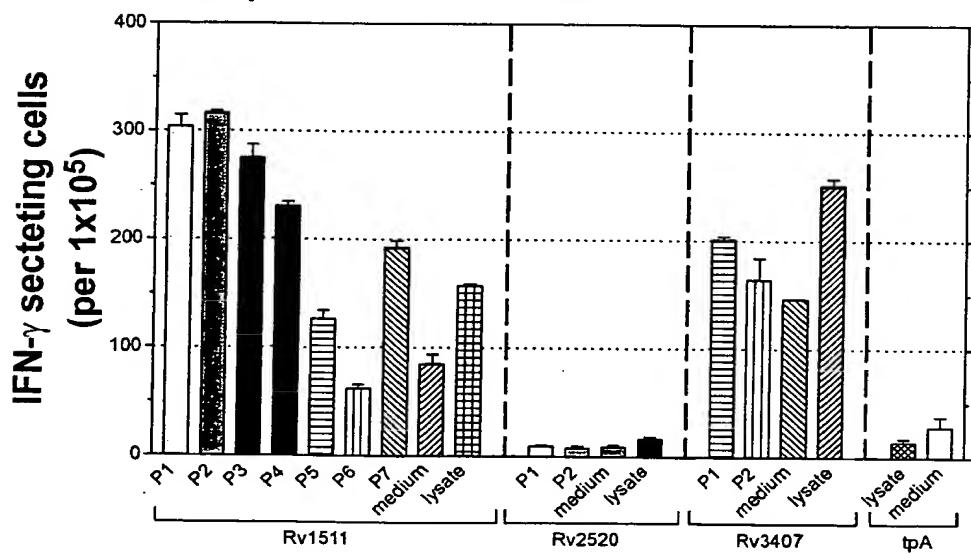


Fig. 4